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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,755	11/28/2000	Hans-Michael Wenz	7414.0020-03	8421

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 04/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,755	WENZ, HANS-MICHAEL	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2006* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *131-144* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *131-144* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 15, 2006 has been entered.

Status

2. Claims 131-144 are pending.

Claims 131-144 are rejected.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Claim Interpretation

3. In the claims, the term "addressable support specific portion" is interpreted as a nucleic acid that can bind a complementary nucleic acid probe. Any nucleic acid sequence whatsoever can meet this limitation since any nucleic acid sequence can hybridize to the complementary sequence by Watson-Crick base pairing.

Claim Rejections - 35 USC § 102

4. The rejections under 35 U.S.C. 102(b) as being anticipated by Whitcombe et al (GB 2,312,747) are withdrawn in view of the amendment.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 131-135 and 141-144 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jenkins (APMIS (1991) 99:667-673) in view of Grossman et al (U.S. Patent 5,514,543).

Jenkins teaches a composition comprising

(i) a plurality of different amplification products drawn to different loci (see figure 2, page 669, where multiple different HPV types were amplified and the probes used hybridize to different physical areas of the HPV genome as shown in figure 1) which comprise;

(a) a first primer specific portion (see page 668, column 1, where common primers are used),

(b) a second primer specific portion (see page 668, column 1, where a second primer specific region is present)

(c) and an addressable support specific portion, between the primer specific portions that is different for each of the amplification products (see figure 1, where each amplification product includes a distinct HPV region) and

(ii) at least two different probes for detection of the different amplification products, (see figure 1) which further comprises:

(a) a tag complement for specifically binding the addressable support specific portion of one of the plurality of different amplification products (See figure 1, where at least three different probes to different HPV types are present),

The amplification products of Jenkins will result in "addressable support specific portions" which are the third regions between the primers, which comprise regions of 15-35 nucleotides in length, which are not complementary with the different loci. For example, the region marked 4 in Hpv6b is 20 nucleotides in length and is not complementary with the other loci in HPV11, HPV16, HPV18 and HPV33. The claim lacks a requirement that the amplification product's addressable support region is not complementary to itself.

With regard to claim 135, Jenkins teaches three different probes (see figure 1).

With regard to claims 132, 137, 142, all of the addressable support specific portions are substantially the same length (see figure 1),

With regard to claims 134, 139, 144, the second primer specific portion is the same for each different amplification product (see figure 1).

With regard to claims 136 and 140, these claims requires that the sequence specific mobility modifiers do not cross hybridize to the same addressable support specific portion. The probes of Jenkins will not cross hybridize since they are drawn to different sequences (see figure 1).

Jenkins does not teach a tail which imparts to each mobility modifier a distinct mobility relative to the other mobility modifiers.

Grossman expressly teaches a method for detection of amplified nucleic acids with unique sequences (see figure 19) with the steps of:

combining the one or more amplification products with at least two different sequence-specific mobility-modifiers, wherein each different mobility-modifier is capable of sequence-specific binding to a different addressable support-specific portion (see column 22, lines 10-17) and comprises (a) a tag complement for specifically binding the addressable support- specific portion of one of the one or more amplification products (see column 22, lines 10-17), and (b) a tail which imparts to each mobility modifier a mobility that is distinctive relative to the mobilities of one or more other of said at least two different mobility-modifiers in a mobility-dependent analysis technique (see column 22, lines 28-32),

removing mobility-modifiers that are not sequence-specifically bound to the one or more amplification products from mobility-modifiers that are sequence-specifically bound to the one or more amplification products (see column 22, lines 24-26),

releasing the sequence-specifically bound mobility-modifiers from the one or more amplification products (see column 22, lines 26-27),

subjecting the released mobility-modifiers to a mobility-dependent analysis technique (see column 22, lines 30-32); and

detecting the one or more target sequences in the sample by detecting distinctive positions of the mobility-modifiers (see column 22, lines 30-32).

With regard to claims 133, 138,143, Grossman teaches that each of the probes has a label (see abstract, for example).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the mobility modifiers of Grossman with the probe detection method of Jenkins in order to obtain advantages suggested by Grossman that the method permits "a rapid, single assay format for detecting the presence or absence of multiple selected sequences in a polynucleotide sample (see column 2, lines 61-63)." An ordinary practitioner would have been motivated to use the mobility modifiers of Grossman in oder to permit more accurate and simple single assay detection of the different HPV types of Jenkins.

8. Claims 131-144 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitcombe et al (GB 2,312,747) in view of Grossman et al (U.S. Patent 5,514,543).

Whitcombe teaches a composition of claims 131 and 141 comprising:

(i) a plurality of different amplification products drawn to different loci (see page 7, lines 6-25, where Whitcombe teaches that the ARMS based technique can be used "to detect more than one suspected variant nucleotide in the same sample" and see page 13, lines 23-31, where Whitcombe teaches that the system can be multiplexed by use different pairs of fluorophores) which comprise;

(a) a first primer specific portion (see figure 9 and table 1, where common first primer regions are used and see page 4, lines 22-25 "primers which are genome specific at their 3' termini but which carry a detector region and common extensions (tags) at their 5' termini"),

(b) a second primer specific portion (see figure 9 and table 1, where common first primer regions are used and see page 4, lines 22-25 "primers which are genome specific at their 3' termini but which carry a detector region and common extensions (tags) at their 5' termini")

(c) and an addressable support specific portion, between the primer specific portions that is different for each of the amplification products (see figure 9 and table 1, where common first primer regions are used and see page 4, lines 22-25 "primers which are genome specific at their 3' termini but which carry a detector region and common extensions (tags) at their 5' termini")

and

(ii) at least two different probes for detection of the different amplification products, (see figure 9 and page 13, lines 23-31, where Whitcombe teaches multiplexing and page 20, lines 16-18, where two different probes were used) which further comprises:

(a) a tag complement for specifically binding the addressable support specific portion of one of the plurality of different amplification products (page 4, lines 22-25 and figure 9, for example),

(b) a "tail" which imparts to each mobility modifier a mobility that is distinctive (see page 20, Cystic fibrosis example, lines 16-18, where the probes are differentially labeled, one with FAM and one with TET, which will impart to each probe a distinct mobility. Further, see page 13, lines 23-25, where Whitcombe teaches that different pairs of fluorophores are used for each multiplexed probe, where each different fluorophore will necessarily and inherently impart distinct mobility to the probe).

The amplification products of Whitcombe will result in "addressable support specific portions" which are the third regions between the primers, which comprise regions of 15-35 nucleotides in length, which are not complementary with the different loci.

With regard to claim 136, Whitcombe expressly teaches multiplex amplification of different target sequences from the same genome (see page 7, lines 13-15, where Whitcombe discusses "screening a single sample of DNA or RNA for a battery of

inherited conditions such as genetic disorders, predispositions and somatic mutations leading to various diseases".)

With regard to claim 135, Whitcombe teaches multiplexing different probes in a battery of inherited conditions (see page 7, line 14, and in any case where there is a mutation, such as the Cystic Fibrosis Delta F508 tested at page 20, that locus will result in two different amplification products, one with the mutation and one without) and Whitcombe also expressly teaches detection of multiple close, but different alleles at page 8, lines 27-28 discussing analysis of "inherited or infectious disease where the potential variant nucleotides are closely spaced") as well as detection of multiple alleles at a single locussuch as in Cystic Fibrosis (see page 9, lines 13-19).

With regard to claims 132, 137, 142, all of the addressable support specific portions are substantially the same length (see figure 9 and table 1, where all of the exemplified addressable support specific regions are nearly identical in length such as T2120 being 30 nucleotides and T4029 also being 30 nucleotides).

With regard to claims 133, 138 and 143, Whitcombe teaches labeling the mobility modifier (see page 20, lines 16-18 and see page 2, lines 11-20, where Whitcombe expressly teaches a detector species which is labeled).

With regard to claims 134, 139, 144, the second primer specific portion is the same for each different amplification product (see figure 9 and table 1 and page 4, lines 23-24 where the primers share "common extension (tags) at their 5' termini").

With regard to claim 140, Whitcombe expressly teaches unique addressable regions, termed detector regions by Whitcombe (see figure 9 and page 2, lines 20-22).

Whitcombe does not teach a tail which imparts to each mobility modifier a distinct mobility relative to the other mobility modifiers.

Grossman expressly teaches a method for detection of amplified nucleic acids with unique sequences (see figure 19) with the steps of:

combining the one or more amplification products with at least two different sequence-specific mobility-modifiers, wherein each different mobility-modifier is capable of sequence-specific binding to a different addressable support-specific portion (see column 22, lines 10-17) and comprises (a) a tag complement for specifically binding the addressable support- specific portion of one of the one or more amplification products (see column 22, lines 10-17), and (b) a tail which imparts to each mobility modifier a mobility that is distinctive relative to the mobilities of one or more other of said at least two different mobility-modifiers in a mobility-dependent analysis technique (see column 22, lines 28-32),

removing mobility-modifiers that are not sequence-specifically bound to the one or more amplification products from mobility-modifiers that are sequence-specifically bound to the one or more amplification products (see column 22, lines 24-26),

releasing the sequence-specifically bound mobility-modifiers from the one or more amplification products (see column 22, lines 26-27),

subjecting the released mobility-modifiers to a mobility-dependent analysis technique (see column 22, lines 30-32); and

detecting the one or more target sequences in the sample by detecting distinctive positions of the mobility-modifiers (see column 22, lines 30-32).

With regard to claims 133, 138,143, Grossman teaches that each of the probes has a label (see abstract, for example).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the mobility modifiers of Grossman with the probe detection method of Whitcombe in order to obtain advantages suggested by Grossman that the method permits "a rapid, single assay format for detecting the presence or absence of multiple selected sequences in a polynucleotide sample (see column 2, lines 61-63)." An ordinary practitioner would have been motivated to use the mobility modifiers of Grossman in oder to permit more accurate and simple single assay detection of the different alleles of Whitcombe in a multiplex format as desired by Whitcombe.

Response to Arguments

9. Applicant's arguments filed March 15, 2006 have been fully considered but they are not persuasive.

Applicant argues that the amendment, in which a "complementary" requirement is imposed on the loci and a length limitation is imposed on the loci, overcomes the Jenkins in view of Grossman 103 rejection. This argument is not found persuasive because, as now noted in the rejection, the amplification products of Jenkins will result

in "addressable support specific portions" which are the third regions between the primers, which comprise regions of 15-35 nucleotides in length, which are not complementary with the different loci. For example, the region marked 4 in Hpv6b is 20 nucleotides in length and is not complementary with the other loci in HPV11, HPV16, HPV18 and HPV33. The claim lacks a requirement that the amplification product's addressable support region is not complementary to itself.

As noted previously, even using the definitions provided by Applicant in response (see page 12 of eDAN document filed 8/01/05, where locus is defined as "the particular site of something, a location" and page 18, where locus is defined as "The position of a gene on a chromosome"). In this case, the oligonucleotide is at different particular sites in the different HPV subtypes and the specific position of the site itself differs in each of the different viral genomes. Thus, the oligonucleotides of Jenkins amplify different "loci" within the broadest reasonable interpretation of that claim as informed by the dictionaries cited by Applicant and in view of the absence of any definition of loci in the specification. Those different loci differ in complementarity and would not be complementary with each other and therefore are "not complementary with the different loci".

The new 103 rejection over Whitcombe et al (GB 2,312,747) in view of Grossman is necessitated by Applicant's amendment to the claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637
9/10/06